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KATE H MURASHIGE
MORRISON & FOERSTER
3811 VALLEY CENTRE DRIVE
SUITE 500
SAN DIEGO, CA 92130-2332

EXAMINER
WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
1639	34

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/284,107	LOGTENBERG ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *2,4,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-10 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Upon reconsideration of the finality of the last Office action, (11/26/02) and telephonic conversation between SPE Wang and Kawai Lau on 5/7/03, the finality of that action is withdrawn.

Status of Claims

Claims 1-20 are pending in the application.

Claims 2, 4, 11-12 are withdrawn from consideration as being drawn to non-elected invention.

Claims 1, 3, 5-10 and 13-20 are under examination.

Specification

The disclosure is objected to because of the following informalities: Typographical errors too numerous to mention specifically. Example of these errors are: "respons" and "loose" at page 3, line 6 and line 16, respectively; "antibo dy", "pac kage"; "contac ted" at page 5, lines 1, 2, 3, respectively and (1996**?**), page 14, line 35. "Legends to the figures" should be changed to a BRIEF DESCRIPTION OF THE DRAWINGS.
"Roomtemperature" at page 16, line 6 should be two words.

Appropriate correction is required.

Applicants are requested to check for other typographical errors since they are ***too numerous to mention specifically***.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5-10 and 13-20 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the last Office action, page 3, paragraph 10.

Response to Arguments

Applicants argue that the present invention may be viewed in light of existing knowledge concerning phage display technology in general. Applicants cite claim 1 of the USP 5,837,500. In response, each case has to be treated on its on merit. Applicants further argue that the claims have been amended to recite the particular peptides for display. In response, these peptides(?) are not particular since immunoglobulin heavy and light chains, scFv, Fab, VH, VL or disulfide bridged Fv can be any antibody that contains these

peptides. However, the specification discloses a specific antibody of scFv. But fails to describe whether this specific antibody (scFv) can be extrapolated to any other antibodies containing any scFV, Ig heavy chain, Ig light chain pair, single chain antibody fragment, VH, VL, FAV, Fv and disulfide bridge Fv. The specification does not contain any other teachings of specific antibodies or any of the specific peptides besides scFV. This is only one of the numerous undefined variables of the broad claimed invention. The claims recite for too numerous undefined variables, conditions that apply to these variables and other unpredictable effects and/or variables. The unpredictability in the art is recognized, no less, by applicants at page 23, lines 21-25 of the specification. Applicants forewarned that in the practice of the method using the bi-specific antibodies from phage antibody, care should be taken in restricting the number of selection rounds on the rod-bound peptides to ensure enrichment for binders but to prevent loss of diversity by over selection. Furthermore, at page 17,lines 18- 20, applicants state that scFv preparations instead of phage preparations were used because the latter generated a high background in ELISA. If applicants have already encountered such difficult situations for a very specific peptide and target how much more for one skilled in the art, given the limited

guidance in the specification? As a skilled in the art knows such diversity is only one of the critical element for the successful practice of the claimed method. The broad claimed invention is nothing more than an invitation to experiment. [Limiting the claims to the antibodies and antigen recited therein will obviate this rejection. The specificity reactions of antibodies-antigen are notoriously well known in the art].

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5-10 and 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claim 1 is confusing. The preamble recites for a peptide capable of binding to a proteinaceous target. The body of the claims does not define a proteinaceous target and a peptide. Rather, the body of the claim recites oligopeptides derived from the proteinaceous target and a peptide as the protein single chain antibody fragment (scFv) and the other

recited antibody protein fragments. Claim 1 is being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step by which the oligopeptides are derived and the step of identifying whether binding occurs thus creating a gap between the step of displaying, synthesizing and identification thereof. It is not clear, within the claimed context, the method by which the oligopeptides are derived, the source from which it is derived. The disclosure does not recite "synthesizing ***oligopeptides*** derived from the proteinaceous target on a solid phase". It recites at page 7 "synthesizing ***sets*** of oligopeptides.." (Emphasis added). It is therefore unclear as to the metes and bounds with respect to the length, number and kind of oligopeptides synthesized in the solid phase. It is not clear within the claimed context the difference between an oligopeptide or a peptide. Also, it is not clear how simply the contacting step is able to identify binding occurrence. "The surface of a replaceable display package" lacks antecedent support. The term "capable" fails to ascertain the claimed invention with precision. It is not clear whether binding positively occurred or not. In the context of the claimed invention, it is not clear as to the difference between a single chain antibody fragment and the acronym scFv.

B). Claim 3 is confusing and rejected basically for the same reasons as claim 1, above. Furthermore, it is not clear as to the basis by which a peptide is considered a "candidate" peptide, especially in the absence of positive recitation in the specification.

C). Claims 7 and 15 are confusing and broaden the base claim which does not recite for a gene or genetic sequence in the method. The preamble "A" should be amended to -The- as the method has antecedent support from the base claim method. See also claims 5-6, 8-10 and 13-18.

D). Claims 8 and 16 do not further limit the base claim 1 and 3. The limitation in claim 8 is already in claim 1 or claim 3, respectively.

E). Claims 10 and 18 are indefinite as to the additional step. The base claim does not recite for a sample containing oligopeptides.

F). Claims 19 and 20 are confusing and inconsistent in the recitation that the proteinaceous target is a protein. Claims 1 and 3 recite for a method by which the target is an oligopeptide derived from protein target. There is no method step recited for a protein as the target. Also, these claims do not further limit the base claim, which already recites that the target is a proteinaceous target.

Response to Arguments

Applicants argue that page 7,lines 30-33 supports "target protein" as opposed to a "proteinaceous target or antigen". Applicants state that the scope of proteinaceous target or antigen includes (1) targets and antigens that are composed of both protein component and a non-protein component as well as (2) targets and antigens that are comprised only of protein. In response, a review of the cited section does not recite for the argued non-protein components and is unclear as to the meaning of the non-protein components. Applicants' arguments are not commensurate in scope with the claims which does not define the argued non-protein components.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the method of claim 3 is not positively disclosed in the specification. [Note although claim 3 and the different antibodies are recited in the original claims however, the original specification does not positively disclose e.g., claim 3, specifically as to a candidate peptide].

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as anticipated by Barsomian (WO 95/15982) for reasons advanced at page 6, paragraph 18 of the last Office action.

Response to Arguments

Applicants argue that Barsomian does not disclose the act of directly synthesizing oligopeptides on a solid phase. But admit that Barsomian describes the immobilization of a "single target antigen" on an insoluble carrier. It is argued that this is not the same as synthesizing multiple oligopeptides on a solid phase. In response, Barsomian discloses at page 8, lines 7-18 that target epitope refers to "epitopes". Therefore, Barsomian discloses multiple epitopes of a target antigen. The claims as broadly interpreted reads on Barsomian's disclosure of antigen containing multiple epitopes synthesized on a solid phase. One having ordinary skill in the art knows that these

epitopes are discrete oligopeptides present in antigen to which antibodies specifically bind (and not to the whole antigen). It is further argued that even assuming that the act of immobilizing a whole antigen was inherently the same as synthesizing a polypeptide on a solid phase, such immobilizing would still not be of more than one oligopeptide derived from a proteinaceous target or antigen as recited in the claims. This is not commensurate in scope with the claims, which do not recite more than one oligopeptide, and unclear as to the numbers of oligopeptide encompassed by said "more than one". Barsomian discloses more than one epitopes of the antigen.

Claims 1, 3, 5-10 and 13-20 are rejected under 35 U.S.C. 102(b) as anticipated by Kruif et al (J. Mol. Biol.) for reasons set forth at pages 7-8, paragraph 20 of the last Office action.

The response above is incorporated herein since applicants merely present the same arguments above. Attention is directed to page 102 of the Kruif reference which recites "these results suggest that the A2 domain is less accessible to phabs when the would protein is used for selection and that additional specificities can be obtained by using ***portions*** of a molecule for selection..." (Emphasis added).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5-10 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Barsomian or Kruif above in view of Middledorp et al (U.S. 5,424,398). [This rejection is based on the claim interpretation that the oligopeptides are sets separately synthesized on the solid support].

Each of Barsomian and Kruif is discussed above. Each of these references does not positively synthesizing multiple individual oligopeptides on the support. However, Middleldorp discloses at col. 7,line 18 up col. 9, line 22 the synthesis of individual antigens or oligopeptides on solid support using the Geysen method. Middeldorp further discloses at col.4, lines 34-50 that the present EBV specific serodiagnosis is accomplished by subjective immunofluorescence tests. Progress to more simple and uniform diagnosis (e.g. ELISA) is hampered because bulk

production and purification of viral antigens is not possible using standard virus producing cell lines. This was only achieved by using alternatively prepared EBV antigen(s). These EBV antigens could be prepared with either genetic engineering techniques or synthetic peptide techniques. Middeldorp further discloses that for the development of a specific and sensitive method to enable a

reliable diagnosis to be made in various phases of the infection with EBV it is of great importance to identify immuno-dominant viral proteins and epitopes thereof.

Accordingly, it would have been obvious to one having ordinary skill in the art to synthesize multiple (sets) of oligopeptides in the method of Barsomian or Kruif in the manner as taught by Middeldorf. The advantages derived in using sets of oligopeptides would provide the motivation to employ sets of oligopeptides. Barsomian or Kruif already suggests that fragments of oligopeptides can be used in the methods.

Claims 1, 3, 5-10 and 13-20 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Burnie et al (Infection and Immunity, 1996).

Burnie discloses a method by which a peptide as antibody can be identified by binding to an fragments of antigens

comprising preparing a phage antibody display and contacting these phage with different sets of antigens specific for S. oralis infection. Accordingly, the specific process steps of Burnie anticipate or render obvious the broad claimed invention that is subject to several interpretations. [When the interpretation of the claim(s) is or may be given one interpretation, a rejection under 35 U.S.C. 102 is appropriate and given another interpretation, a rejection under 35 U.S.C. 103(a) is appropriate. See MPEP § § 2111- 2116.01.].

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
May 23, 2003